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| APPLICATION NO.                  | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|----------------------------------|-------------|----------------------|---------------------|------------------|
| 10/533,806                       | 05/05/2005  | Hashime Kanazawa     | 2005_0741A          | 8202             |
| 513                              | 7590        | 10/14/2008           | EXAMINER            |                  |
| WENDEROTH, LIND & PONACK, L.L.P. |             |                      | DESAI, RITA J       |                  |
| 2033 K STREET N. W.              |             |                      |                     |                  |
| SUITE 800                        |             |                      | ART UNIT            | PAPER NUMBER     |
| WASHINGTON, DC 20006-1021        |             |                      | 1625                |                  |
|                                  |             |                      |                     |                  |
|                                  |             |                      | MAIL DATE           | DELIVERY MODE    |
|                                  |             |                      | 10/14/2008          | PAPER            |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                        |                     |  |
|------------------------------|------------------------|---------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |  |
|                              | 10/533,806             | KANAZAWA ET AL.     |  |
|                              | <b>Examiner</b>        | <b>Art Unit</b>     |  |
|                              | Rita J. Desai          | 1625                |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 19 August 2008.

2a) This action is **FINAL**.                            2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1 and 5 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1 and 5 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.

    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

    Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

- Certified copies of the priority documents have been received.
- Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
- Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

|  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ .                                    |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ .  | 6) <input type="checkbox"/> Other: _____ .                        |

**DETAILED ACTION**

***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/19/08 has been entered.

Applicants have amended their claims and only claims 1 and 5 are pending.

Applicants arguments regarding the rejection under 35 USC 103(a) over EP '840 and US'610 are not found to be convincing.

The comparative data given in the declaration indicates that the results were conducted using Nicholson et al method. Which is different than that of the prior art .

Besides EP '725 the comparative data obtained by the Probit Method on page 16 has IC50 data for PDE IV. It ranges from .06 to 2.2. which differs by a factor of 4.

| Test Compounds | Inhibition of PDE isoenzymes (IC <sub>50</sub> ; μM) |      |      |          |      |
|----------------|--|------|------|----------|------|
|                | I  | II   | III  | IV       | V    |
| Example No. 2  | >100   | >100 | >100 | 0.11     | 16   |
| Example No. 3  | >100   | >100 | >100 | 1.2      | 3.9  |
| Example No. 5  | 22   | >100 | 60   | 0.06     | 13   |
| Example No. 6  | >100   | >100 | >100 | 0.16     | 16   |
| Example No. 7  | >100   | >100 | >100 | 1.3      | 4.7  |
| Example No. 8  | >100   | >100 | >100 | 0.44     | >100 |
| Example No. 10 | >100   | 52   | 24   | 1.5      | 13   |
| Example No. 13 | 62   | 60   | 94   | 1.2      | 13   |
| Example No. 14 | 63   | 85   | 59   | 1.5      | 5.1  |
| Example No. 15 | 100  | 47   | 48   | 3.4      | 8.7  |
| Example No. 16 | 98   | 63   | 69   | 1.9      | 7.4  |
| Example No. 17 | >100   | >100 | >100 | 2.2      | >100 |
| Example No. 23 | >100   | >100 | >100 | 1.2      | >100 |
| Rosipram       | >100   | >100 | >100 | 0.78-3.2 | >100 |

Thus varying of results with the various substitutents upto 4 times is not considered to be unexpected.

The inhibition rate is considered to be different than IC<sub>50</sub> values. Applicants are comparing 2 different types of data.

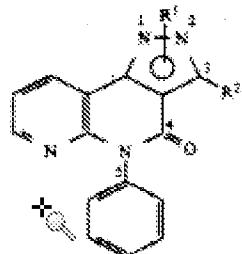
So applicants arguments that the difference of activity for that one particular compounds by one specific method varies by 3 times is considered to be unexpected is not found to be convincing.

Hence the rejection still stands.

The rejection is being repeated here.

The rejection of claims 1-24 ( now 1-6, 8-15, 19-24) under 35 USC 103 over EP 0526840 and US 5281610 however still stands. Applicants declaration does have some data for one compound. Just the phenyl.

The prior art also has thienyl group and an alkyl chain . see below.



wherein  $R^1$  is represents hydrogen, lower alkyl, alkyl, or substituted or unsubstituted aryl.  $R^2$  represents hydrogen, lower alkyl, thienyl, substituted or unsubstituted aryl, hydroxy or amino, or a pharmaceutically acceptable salt thereof.

The compound possesses antiinflammatory effect, immunosuppressive effects, broncho-dilatory effect and hair growth-stimulative effect.

The reference also teaches that they have bronco dilatory effect. Applicants claims are also drawn to the same treatment, "bronchial asthma" . Applicants argument that the A group with the linkage is a distinct feature for the acquisition of PDE IV inhibitory activity is not understood. The prior art compounds have the same activity as bronco dilators. Applicants claims are also drawn to treating asthma and such which are also treated by bronchodilators.

Applicants arguments with respect to the advantages is also not convincing. The Sazuki reference may be just silent as to the type of inhibition, but it does treat the same disorder, Broncodilation, which is what is required to treat a number of bronchial disorders.

Applicants further argue that it has an unexpected increase in PDE IV inhibition. Applicants declaration does not compare all the closest art compounds and is not convincing.

WO 01/42244 and EP 1236 725, Aotsuka et al discloses the A group on a similar naphthyridin -2(1H)-one derivative. These are PDE IV inhibitors too.

These references have a methylene group with the A substituent. ( these references were provided in the IDS and are used only to overcome applicants arguments that the novelty of the activity is due to the CH2-A group)

Thus motivation to modify the US '610 compounds can also come from the teaching of WO '244 and '725 which have the substituent similar to the one at the 3 position.

Thus the rejection still stands.

***Conclusion***

Claims 1 and 5 still stand rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rita J. Desai/  
Primary Examiner, Art Unit 1625

R.D.  
October 9, 2008